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**METABOLIC OUTCOMES AFTER BARIATRIC SURGERY: EFFECTS ON  
DIABETES, DYSLIPIDEMIA AND HIGH BLOOD PRESSURE**

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## METABOLIC OUTCOMES AFTER BARIATRIC SURGERY: EFFECTS ON DIABETES, DYSLIPIDEMIA AND HIGH BLOOD PRESSURE

### REVISÃO BIBLIOGRÁFICA

Dissertação de Candidatura ao grau de Mestre em Medicina submetida ao  
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## ABBREVIATION LIST

**ADA** – American Diabetes Association  
**BPD** – Biliopancreatic Diversion  
**BMI** – Body Mass Index  
**dBp** – Diastolic Blood Pressure  
**DLP** – Dyslipidemia  
**DSIT** – Diverted Sleeve Gastrectomy with Ileal Transposition  
**FPG** – Fasting Plasma Glucose  
**GB** – Gastric Banding  
**HbA1C** – Glycated Hemoglobin  
**HBP** – High blood pressure  
**HDL** – High Density Lipoproteins  
**HOMA-IR** – Homeostatic Model Assessment of Insulin Resistance  
**ILMI** – Intensive Lifestyle and Medical Intervention  
**LDL** – Low Density Lipoproteins  
**LWLI** – Intensive Lifestyle Weight Loss Intervention  
**MAP** – Mean Arterial Pressure  
**NEFA** – Non-Esterified Fatty Acids  
**OR** – Odds Ratio  
**RCT(s)** – Randomized Controlled Trial(s)  
**RR** – Risk Ratio  
**RYGB** – Roux-en-Y Gastric Bypass  
**sBP** – Systolic Blood Pressure  
**SG** – Sleeve Gastrectomy  
**SIPS** – Stomach Intestinal Pylorus Sparing  
**SOS** – “Swedish Obese Subjects”  
**T2DM** – Type 2 Diabetes Mellitus  
**TG** – Triglycerides  
**VLDL** – Very Low Density Lipoproteins  
**WHO** – World Health Organization  
**%EWL** – Excess Weight Loss Percentage  
**%TWL** – Total Weight Loss Percentage

## ABSTRACT

**Introduction:** Type 2 diabetes *mellitus*, high blood pressure and dyslipidemia are important cardiovascular risk factors associated with obesity. Bariatric surgery is effective in treating obesity and may influence the associated comorbidities, having been already included in the treatment recommendations for type 2 diabetes *mellitus*.

**Objectives:** This review aimed to summarize the known effects of bariatric surgery on these 3 important comorbidities associated with obesity.

**Methods:** PubMed was the main source, namely the MeSH database. Out of 945 articles published in the last 5 years, 49 articles were selected. The articles were divided in 3 groups for separate analysis of each comorbidity.

**Conclusion:** Bariatric surgery has great potential in managing obesity related comorbidities. The outcomes are best established for type 2 diabetes *mellitus* than for high blood pressure and dyslipidemia, but bariatric surgery has shown superiority to optimal medical treatment in all.

**Key Words:** Bariatric surgery, Obesity, Type 2 diabetes *mellitus*, High blood pressure, Dyslipidemia, Metabolic outcomes

## RESUMO

**Introdução:** Diabetes *mellitus* tipo 2, hipertensão arterial e dislipidemia são importantes factores de risco cardiovascular associados à obesidade. A cirurgia bariátrica é eficaz no tratamento da obesidade e pode influenciar as comorbilidades associadas, tendo já sido incluída nas recomendações para o tratamento de diabetes *mellitus* tipo 2.

**Objectivo:** Esta revisão bibliográfica tem como objectivo sumariar os efeitos conhecidos da cirurgia bariátrica nestas 3 importantes comorbilidades associadas à obesidade.

**Métodos:** o PubMed foi a principal fonte de informação, nomeadamente a base de dados MeSH. De 945 artigos publicados nos últimos 5 anos, 49 foram seleccionados. Os artigos foram divididos em 3 grupos para análise independente de cada comorbilidade.

**Conclusão:** A cirurgia bariátrica tem grande potencial na abordagem de comorbilidades associadas à obesidade. Os resultados estão melhor demonstrados para a diabetes *mellitus* tipo 2 do que para a hipertensão arterial e dislipidemia, mas a cirurgia bariátrica mostrou superioridade ao tratamento médico optimizado em todas as comorbilidades.

**Palavras-chave:** Cirurgia bariátrica, Obesidade, Diabetes *mellitus* tipo 2, Hipertensão arterial, Dislipidemia, Alterações metabólicas

## INTRODUCTION

Diabetes *mellitus*, HBP and DLP are cardiovascular risk factors with substantial impact and highly prevalent worldwide[1, 2] – according to the WHO the global prevalence of diabetes *mellitus* is around 8.5%[1], HBP is estimated to have a prevalence around 40% among adults[2] and DLP is estimated to be present in around 39% of the world's adult population[2]. Obesity is associated to a higher risk of T2DM, HBP, DLP.[1, 3-7] For instance, HBP is the most common comorbidity in obese patients[8] and about 40% of morbidly obese patients have DLP.[9]

Lifestyle modification and medical therapy are the main tools available for managing obesity, T2DM, HBP and DLP but appropriate control is not easy to achieve, with only a minority of patients achieving control of all these diseases both individually and simultaneously.[5, 10, 11]

Bariatric surgery achieves substantial and sustained weight loss, it can improve the associated comorbidities[3, 5, 6, 12, 13] and after bariatric surgery there is a reduction in cardiovascular mortality.[9] Currently, the two most commonly used bariatric procedures are RYGB and SG[14, 15], with a higher increase in the use of SG than RYGB in recent years.[15-17] RYGB is considered the *gold standard* in bariatric surgery.[8, 17, 18] Other common procedure is GB[19], but its use has been decreasing in recent years.[15] There are some new procedures in study, including endoscopic procedures that are less invasive, but they are still under investigation before they can be considered as valid treatment options for obesity and its comorbidities.[15, 19]

The present recommendations for using bariatric surgery include all patients with BMI > 40 kg/m<sup>2</sup>. [20] For patients with lower BMI, most agree that in patients with BMI > 35 kg/m<sup>2</sup> and at least 1 obesity-related comorbidity, surgery should be offered, mainly if that comorbidity is not well controlled with medical therapy.[20] Not all recommendations agree, but some suggest surgery for patients with BMI 30–35 kg/m<sup>2</sup> and a comorbidity poorly controlled with medical therapy predicted to respond to surgery.[20] As a treatment for T2DM, bariatric surgery follows these recommendations and it should be offered to diabetic patients with BMI ≥ 35 kg/m<sup>2</sup>[12, 14, 17, 21], especially if poorly controlled with optimal medical treatment, while for patients with mild obesity (30 kg/m<sup>2</sup> ≤ BMI < 35 kg/m<sup>2</sup>) the recommendations aren't unanimous.[14] The BMI thresholds in these recommendations need to be adjusted for Asian populations[21] – BMI thresholds are lower in these populations (≈2.5 kg/m<sup>2</sup>).

Therefore, bariatric surgery may be an important therapeutic approach for obesity and obesity related comorbidities. This review aims to summarize the known effects of bariatric surgery on 3 important comorbidities – T2DM, HBP and DLP.

## METHODS

A search was performed on *PubMed*, using the MeSH Database. The following formula was used: ("Bariatric Surgery"[Mesh] OR "Bariatric Medicine"[Mesh]) AND ("Diabetes Mellitus, Type 2"[Mesh] OR "Hypertension"[Mesh] OR "Dyslipidemias"[Mesh])."

The articles were filtered to include only studies in the Human species and published in the last 5 years. This search gathered 945 results. Out of these 945 articles, 90 articles were selected after reading the abstract of every article. The main criteria for inclusion were articles in English language and articles on the outcomes of bariatric surgery regarding at least 1 of the 3 selected comorbidities.

After reading the full text of the articles, 49 articles were selected. The remaining 41 articles were excluded for not following the specifications mentioned previously, for not being relevant for the present review and for referring to biochemical or anatomopathological changes after bariatric surgery without specifying the metabolic outcomes associated.

## RESULTS

### T2DM

Bariatric surgery improves glycaemic control (evaluated by the levels of HbA1C), leading to a clinical improvement in the vast majority of patients with T2DM.[3, 5, 10, 14, 18, 19, 22-24] Surgical management of T2DM has proven to be superior to the optimal medical treatment (pharmacological treatment and lifestyle modification therapies currently available).[12, 14, 17, 18, 23, 25-27] Bariatric surgery reduces the need for medication in managing T2DM[10, 14, 23] and, in some cases, achieves remission of the disease.[3, 11, 12, 18, 25] The effect of bariatric surgery on T2DM associated complications (diabetic nephropathy, diabetic neuropathy, diabetic retinopathy...) is not well known.[11]

Remission rates of around 75% have been described for RYGB[14, 28] – up until 2 years after surgery[29] – and bariatric surgery has been shown to have an OR above 8 for T2DM remission compared to optimal medical treatment.[12]

Yan et al.[7] analysed 6 RCTs comparing RYGB with medical treatment for obese patients with T2DM. Regarding T2DM remission, a significant difference was found between the 2 groups (over 55% in the RYGB group vs. no remission in the medical group). The reduction of HbA1C and medication use was also significantly higher in the surgical group but there was no significant difference in the reduction of FPG.

Mingrone et al.[30] randomised 60 patients with BMI  $\geq 35$  kg/m<sup>2</sup> and T2DM for at least 5 years in 3 groups – 1 group underwent BPD, another underwent RYGB and the last group underwent medical treatment. After 5 years of follow-up there was no remission in the medical group and BPD presented a remission rate of over 60%, compared to a remission rate of nearly 40% following RYGB. Independently of remission, over 40% in the RYGB group and almost 70% in the BPD group achieved HbA1C levels  $\leq 6.5\%$  with or without medication, compared to a little over 25% of patients in the medical group. Additionally, over 80% of the patients in the surgical groups achieved HbA1C  $< 7.0\%$  with no or only little use of medication. The use of medication and insulin was significantly lower in the surgical groups.

Yska et al.[27] compared obese (BMI  $> 35$  kg/m<sup>2</sup>) patients with T2DM that underwent different bariatric procedures (RYGB, SG and GB) with a matched control group. The surgical group had an 18-fold increase in the chance of T2DM remission, with a higher chance of remission for RYGB (RR  $> 40$ ), followed by SG (RR  $> 15$ ) and GB (RR  $\approx 7$ ). HbA1C and FPG had significant reductions in the 1<sup>st</sup> year after surgery, compared to the medical group and medication use was significantly lower in the surgical group after 3 years of follow-up.



Two meta-analysis by Cho et al.[16] and Li et al.[8] compared the effects of SG and RYGB on T2DM. Overall, higher rate of remission was reported for RYGB, but no statistically significant difference relatively to SG was found. However, in the paper by Cho et al.[16], when considering only the RCTs included, there was a slight advantage in remission rates 1 year after surgery for RYGB.

Schauer et al.[23] reported 3-year outcomes in 150 obese patients with poorly controlled T2DM ( $\text{HbA1C} > 7.0\%$ ) randomized for RYGB, SG or intensive medical therapy. The primary end-point for this study was  $\text{HbA1C} \leq 6.0\%$  independently of medication use. After 3 years of follow-up, statistically significant differences between the two surgical groups comparing to the medical group were found. This difference was also found for other end-points –  $\text{HbA1C} \leq 6.5\%$  and  $\leq 7.0\%$ . Both surgical procedures achieved bigger, quicker and more sustained reductions in  $\text{HbA1C}$ , FPG and medication use. There were no significant differences in the reductions of  $\text{HbA1C}$  and FPG between patients with  $\text{BMI} < 35 \text{ kg/m}^2$  and patients with  $\text{BMI} \geq 35 \text{ kg/m}^2$ . When comparing the 2 surgical groups, RYGB had lower need of medication than SG, with a higher proportion of patients in the RYGB group not needing any medication. Schauer et al.[31] reported the 5-year outcomes for this population. At that time, the two surgical groups kept statistically significant differences compared to the medical group. Both surgical procedures kept their superiority in inducing reductions in  $\text{HbA1C}$ , FPG and medication use. Reduction of  $\text{HbA1C}$  was not significantly different between patients with  $\text{BMI} < 35 \text{ kg/m}^2$  and patients with  $\text{BMI} \geq 35 \text{ kg/m}^2$ . RYGB also kept a lower need for medication than SG, with a higher proportion of patients in the RYGB group not needing any medication.

Shoar et al.[32] analysed mid and long-term metabolic outcomes for RYGB and SG – Mid-term was considered for follow-up periods from 3 to 5 years and long-term was defined as a follow-up period of 5 years or more. Regarding T2DM remission, no differences were found between the 2 procedures in either follow-up period, with similar remission rates for RYGB and SG in both mid and long-term.

Nosso et al.[33] studied obese patients with T2DM that underwent RYGB or SG. After surgery, both insulin sensitivity and insulin secretion improved similarly for the 2 procedures, and no significant difference was found between both procedures.

Griffo et al.[34] published a paper that evaluated early changes in metabolic parameters, 2 weeks after RYGB and SG. It detected significant reductions in FPG, and insulin resistance (HOMA-IR), also with no significant differences between both surgical procedures.

Liu et al.[35] studied obese patients from a Chinese population who underwent SG. Total T2DM remission rates reached 70% at 5 years of follow-up and optimal glycaemic control was achieved in over 70%, with significant reductions in  $\text{HbA1C}$ .

Courcoulas et al.[36] compared health outcomes in severely obese patients with multiple comorbidities following RYGB and GB after 3 years of follow-up. This paper showed that RYGB had better results than GB in T2DM remission, but both procedures have proved to induce significant improvements in T2DM.

Celik et al.[37] analysed the metabolic outcomes of a different procedure, DSIT, on obese patients ( $\text{BMI} > 35 \text{ kg/m}^2$ ) with T2DM. He detected significant reductions in FPG, HbA1C and postprandial plasma glucose 1 year after surgery.

Several different definitions of T2DM remission have been used[14], mostly including HbA1C levels. This creates a bias in studying the remission rates after bariatric surgery because slight differences in the HbA1C values considered may impact greatly on the remission rates found[12, 14, 26] – for instance, reducing the threshold of remission from HbA1C levels of 6.0% to 5.7% can reduce the remission rates in half.[14] Table I presents an overview of the articles analysed and the main information reported regarding T2DM remission.

Remission of T2DM is dependent of other factors, beginning with the surgical procedure chosen – most studies report the best results for BPD[14, 15, 17, 18, 38] – some modifications of this procedure, like SIPS surgery, have been proposed with good results[15]; RYGB is considered to have good results, even in patients with advanced disease[25], despite having lower remission rates than BPD[14, 18, 38]; SG has lower remission rates than RYGB[11, 12, 14, 17-19, 25], but higher than GB[11, 14, 17, 18, 27] – one of the main advantages of GB is its reversibility[4] and although GB is considered a less invasive method, with smaller chance of complications, there is a high rate of reoperation for adjustment and removal, undermining its other big advantage.[25].

Other factor is the severity of the disease prior to surgery, with lower rates of remission for patients with advanced disease[25] (longer disease duration[3, 11, 12, 14, 18, 39], higher HbA1C[39, 40], lower C-peptide levels[18, 40], preoperative use of insulin[18, 40], ...). Some studies have detected %EWL[3, 11] and BMI[39] as predictors of remission, but others showed that T2DM remission is independent of weight loss[10] and preoperative BMI[26, 39]. Some studies also suggest that older age may reduce the chance of remission.[18, 39, 40] Recently, there are some studies that suggest abdominal circumference as a better predictor for T2DM remission than BMI.[18, 26, 38]

Chen et al.[18] reported the impact of RYGB in T2DM patients and found clinical improvement in over 75% of patients after RYGB surgery. This study identified some factors that influence remission rates, with higher remission detected for higher preoperative C-peptide levels and for lower T2DM duration, age, insulin use, preoperative FPG and preoperative HbA1C. Additionally, lower total cholesterol, TG and LDL and higher HDL were shown to increase remission rates, as well as lower prevalence of HBP. The authors also found that lower waist circumference was associated to higher remission rates, unlike BMI, which didn't significantly alter the remission rates.

Palmisano et al.[39] aimed to identify preoperative predictors of T2DM remission 1 year after RYGB. There was a decrease in HbA1C in all patients, with remission rates around 60% after 1 year of follow-up. The patients were divided in 2 groups according to preoperative HbA1C levels. The cut-off for these groups was the mean preoperative HbA1C (7.8%). The preoperative predictive factors identified were  $\text{BMI} > 30 \text{ kg/m}^2$  and low preoperative HbA1C ( $< 7.8\%$ ).

Panunzi et al.[38] published a meta-analysis that aimed to compare T2DM remission in diabetic patients with BMI  $\geq 35$  kg/m<sup>2</sup> and diabetic patients with BMI  $< 35$  kg/m<sup>2</sup> and also to identify predictors of that remission. The 3 main conclusions of this study were that: 1) bariatric surgery induces similar clinical improvement of T2DM in both BMI groups; 2) the reduction in HbA1C levels is independent of preoperative BMI; and 3) decrease in HbA1C levels is inversely related with abdominal circumference. The study concludes that BMI is not a good eligibility criteria for bariatric surgery.

Another paper by Panunzi et al.[26] merged the SOS study database with 2 RCTs and obtained 2 groups of patients – the 1<sup>st</sup> included obese patients with T2DM that underwent medical treatment and the 2<sup>nd</sup> included obese patients with T2DM that underwent bariatric procedures –, followed for 2 years. Remission rates were significantly higher in the surgical group (over 60% vs. 15% in the medical group). There were no differences for different types of bariatric procedure in both remission and glycaemic control. The overall predictive factors for higher T2DM remission for both groups were younger age, shorter duration of T2DM, lower preoperative FPG and lower preoperative use of medication. When divided in 3 groups according to BMI ( $\leq 35$  kg/m<sup>2</sup>, 35–40 kg/m<sup>2</sup> and  $> 40$  kg/m<sup>2</sup>), there was significant difference between the group with BMI  $\leq 35$  kg/m<sup>2</sup> and the group with  $> 40$  kg/m<sup>2</sup> (OR = 2.9, favourable for BMI  $> 40$  kg/m<sup>2</sup>), but not between BMI  $\leq 35$  kg/m<sup>2</sup> and BMI 35–40 kg/m<sup>2</sup>. This study suggests abdominal circumference could replace BMI as the main eligibility criteria for bariatric surgery.

Park et al.[40] also tried to identify predictors of T2DM remission following RYGB. 4 predictive factors of T2DM remission after RYGB were identified: preoperative C-peptide levels and %TWL after surgery had a direct correlation with T2DM remission, while age in the moment of surgery and preoperative HbA1C levels were inversely correlated with remission. This study proposed a decision tree model (Figure 1) based on the preoperative predictors, and found C-peptide levels to be the most discriminating variable for T2DM remission – in this cohort, C-peptide  $> 2.6$  ng/dL was mandatory to achieve T2DM remission –, followed by BMI and, finally, insulin use

Zenti et al.[41] studied obese patients (mean BMI  $> 45$  kg/m<sup>2</sup>) with T2DM who underwent RYGB, SG and GB and analysed predictors of T2DM remission in that population. Younger age, shorter duration of T2DM and lower HbA1C ( $< 7.0\%$ ) were associated with higher remission rates. Remission rates were lower for GB than for the other procedures, with no significant difference between RYGB and SG.

Article	Type of study	Number of patients	Surgical procedures studied	Remission criteria	Remission rates (%)	Follow-up period
Yan et al.[7]	Meta-analysis	410	RYGB	Not consensual among the studies analysed	≈ 57	1 – 5 years
Mingrone et al.[30]	RCT	60	BPD, RYGB	HbA1C < 6.0% and no medication	50	5 years
Yska et al.[27]	Retrospective	2 450	RYGB, SG, GB	HbA1C < 6.0% and no medication	94.5 <sup>a</sup>	2.4 years <sup>f</sup>
Cho et al.[16]	Meta-analysis	857	RYGB, SG	Not consensual among the studies analysed	73; 80 <sup>b</sup>	1 year
Li et al.[8]	Meta-analysis	18 449	RYGB, SG	HbA1C < 6.5%, FPG < 126 mg/dL and no medication	≈ 77	1.5 – 60 months
Schauer et al.[23]	RCT	137	RYGB, SG	HbA1C ≤ 6.0%	38; 24 <sup>b</sup>	3 years
Schauer et al.[31]	RCT	134	RYGB, SG	HbA1C ≤ 6.0%	29; 23 <sup>b</sup>	5 years
Shoar et al.[32]	Meta-analysis	5 264	RYGB, SG	Not defined	82; ≥ 76 <sup>b</sup>	> 3 years
Nosso et al.[33]	Prospective	33	RYGB, SG	HbA1C < 6.0%, FPG < 100 mg/dL and no medication (complete), HbA1C < 6.5%, FPG < 125 mg/dL and no medication (partial)	> 85; 75 <sup>b</sup>	1 year
Liu et al.[35]	Prospective	140	SG	HbA1C < 6.5%, FPG < 100 mg/dL and 1 year without medication (complete), HbA1C < 6.5%, FPG < 126 mg/dL and 1 year without medication (partial)	70	5 years
Courcoulas et al.[36]	Prospective	2 348	RYGB, GB	Not defined	≈ 68; 29 <sup>c</sup>	3 years
Celik et al.[37]	Retrospective	159	DSIT	Not defined	> 85	18 months <sup>f</sup>
Chen et al.[18]	Meta-analysis	924	RYGB	HbA1C < 5.7%, FPG < 100 mg/dL and no medication	50; 90 <sup>d</sup>	6 – 24 months
Palmisano et al.[39]	Prospective	771	RYGB	Not defined	58	1 year
Panunzi et al.[26]	Meta-analysis	727	BPD, RYGB, SG, GB	FPG < 100 mg/dL and no medication	≈ 65	2 years
Park et al.[40]	Retrospective	134	RYGB	HbA1C < 6.0% and no medication (complete), HbA1C < 6.5% and no medication (partial)	45; 15 <sup>e</sup>	12 months <sup>e</sup>

Table I – Summary of T2DM remission rates found in the articles analysed

a – In this study remission rates was calculated as number of remissions per 1 000 person-years.

b – Remission rates were analysed independently for RYGB (higher value) and SG (lower value).

c – Remission rates were analysed independently for RYGB (higher value) and GB (lower value).

d – Remission rates were analysed separately for preoperative insulin users (lower value) and patients with no prior insulin use (higher value).

e – Remission rates were analysed independently for complete remission (higher value) and partial remission (lower value).

f – Only mean follow-up was reported.

Some authors proposed metabolic scores to define if there is indication for bariatric surgery[10] Some proposed predictive scores of T2DM remission following bariatric surgery, and a few have been validated[40], as the ABCD Score[42] (Table II) – with a range from 0 to 10, with higher chance of T2DM remission for higher scores, validated to Asian populations – and DiaRem Score[43] (Table III) – ranging from 0 to 22, with higher scores corresponding to lower probability of T2DM remission following RYGB.

Variable	Points			
	0	1	2	3
Age (years)	$\geq 40$	$< 40$	–	–
BMI (kg/m <sup>2</sup> )	$< 27$	27–34.9	35–41.9	$\geq 42$
C-peptide (ng/ml)	$< 2$	2–3.9	4–6	$> 6$
T2DM duration (years)	$> 10$	5–10	2–4.9	$< 2$

Table II – ABCD Score[42]

Some studies in patients with lower BMI ( $30 \text{ kg/m}^2 \leq \text{BMI} < 35 \text{ kg/m}^2$ ) have shown that bariatric surgery maintains superiority as a treatment option for T2DM compared to optimal medical treatment in mildly obese patients with T2DM.[12, 18, 25, 44] Some studies report lower remission rates in these patients (up to 50% vs. 75%[14]) when compared with morbidly obese patients ( $\text{BMI} > 40 \text{ kg/m}^2$ )[14], while others show that there's no significant difference.[10, 44] Independently of remission, the changes in FPG and HbA1C after RYGB follow similar patterns in both clusters.[14] Some of these studies, conducted in Asian populations, may induce some bias in recommending bariatric surgery for patients with lower BMI values, because in these populations the BMI thresholds for the classifications of obesity are lower, which means that Asian patients with BMI considered as mild obesity in Western countries may, in fact, correspond to severe or morbidly obese patients.[14]

Cummings et al.[45] published a RCT comparing RYGB with ILMI in obese patients ( $\text{BMI} 30\text{--}45 \text{ kg/m}^2$ ) with T2DM. Remission of T2DM was defined as  $\text{HbA1C} < 6.0\%$  with no use of medication. After 1 year of follow-up, remission rates were significantly different (60% for RYGB vs.  $< 6\%$  for ILMI), with an OR of remission reaching nearly 20 for RYGB compared to ILMI. Reductions in HbA1C and FPG were not significantly different but after RYGB medication use was significantly lower for the surgical group, as well as insulin use (even with higher baseline insulin use in the surgical group).

Age (years)	Points
< 40	0
40–49	1
50–59	2
≥ 60	3
HbA1C (%)	
< 6.5	0
6.5–6.9	2
7.0–8.9	4
≥ 9.0	6
Treatment with insulin	
No	0
Yes	10
Other medications	
No sulfonylureas or insulin-sensitising agent other than metformin	0
Sulfonylureas and insulin-sensitising agent other than metformin	3

Table II – DiaRem Score[43]

Another RCT by Courcoulas et al.[46] compared RYGB and GB with LWLI in obese ( $30 \leq \text{BMI} < 40$ ) patients with T2DM. Partial remission ( $\text{HbA1C} < 6.5\%$  and  $\text{FPG} \leq 125 \text{ mg/dL}$  with no medication) and total remission ( $\text{HbA1C} < 5.7\%$  and  $\text{FPG} \leq 100 \text{ mg/dL}$  with no medication) were assessed. Overall remission (partial or complete) was higher for RYGB than GB (40% vs. 29%) and there was no remission with LWLI. Complete remission was also higher for RYGB (15% vs. 5%). The authors detected no significant difference between obesity classes (Class I –  $30 \leq \text{BMI} < 35$  – vs. Class II –  $35 \leq \text{BMI} < 40$ ) in HbA1C and FPG reductions. There was a lower need for medication in patients that underwent bariatric surgery with a significant number of patients with no use of medication after surgical treatment (72% after RYGB vs. 45% after GB), opposing to no patients without medication after LWLI.

Ikramuddin et al.[47] published a RCT in which 120 patients with BMI  $30\text{--}40 \text{ kg/m}^2$  with T2DM for at least 6 months,  $\text{HbA1C} \geq 8.0\%$  and C-peptide  $> 1.0 \text{ ng/mL}$  were randomized to receive RYGB or medical treatment. In this study, the primary outcome included 3 metabolic parameters –  $\text{HbA1C} < 7.0\%$ ,  $\text{LDL} < 100 \text{ mg/dL}$  and  $\text{sBP} < 130 \text{ mmHg}$ . There was a significant difference in achieving this outcome after 1 year of follow-up (49% after RYGB vs. 19% in the medical group), with an OR of nearly 5, favourable to RYGB. Separate analysis of each parameter of the primary outcome at 1 year of follow-up showed only significant difference regarding HbA1C (75% after RYGB vs. 32% for the medical group), with an OR of 6, also favourable to RYGB. FPG reduction was also higher after RYGB and in the RYGB group there was a lower need for T2DM medication. Another paper by Ikramuddin et al.[48] reported the 2 year outcomes of this RCT. The differences for primary outcome and its parameters found at 1 year follow-up were maintained, with a slight decrease of the number of patients that achieved the primary outcome in both groups. Mean FPG was significantly lower in the RYGB group. 12% of the RYGB group patients that achieved the primary outcome at 2 years were using no medication.

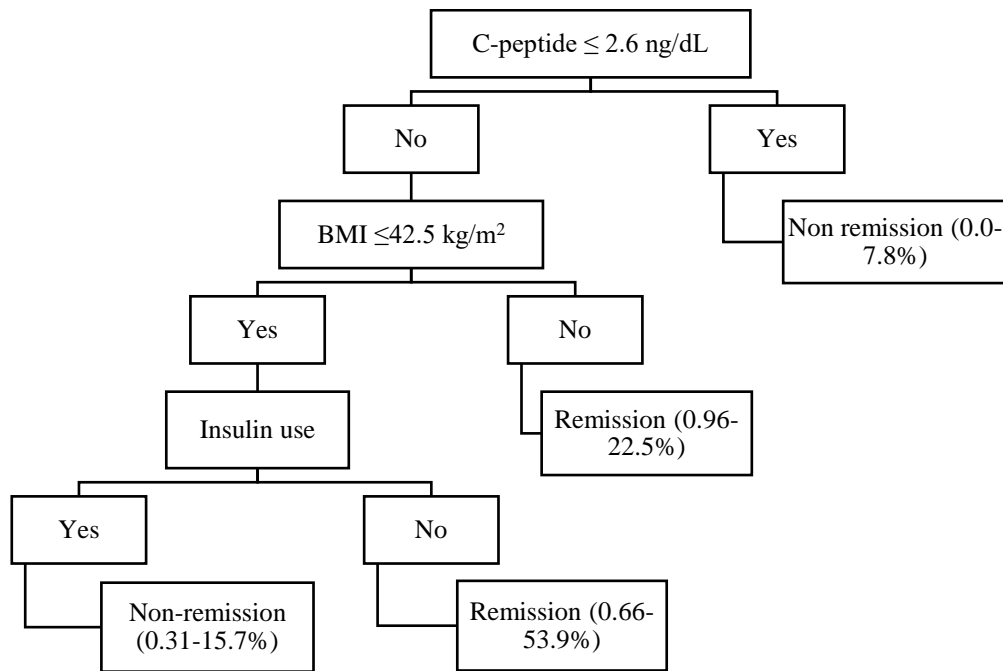


Figure 1 – Decision tree model for T2DM remission following RYGB by Park et al. (2015)[40]

Xu et al.[44] analysed RYGB outcomes in T2DM patients and compared these outcomes between patients with class I obesity and patients with class II or III obesity during 3 years of follow-up. Complete remission was defined as HbA1C < 6.0% and FPG < 100 mg/dL, partial remission was defined as HbA1C < 6.5% and FPG 100–125 mg/dL and good glycaemic control was obtained if HbA1C < 7.0% and no use of medication was mandatory to define each of these end-points. Both obesity class groups showed similar evolution of multiple metabolic parameters. Partial remission was similar in the 2 groups in all points of follow-up. Complete remission was significantly higher for the group with more severe obesity at 1 and 2 years of follow-up, but there was no difference in the 3-year evaluation. HbA1C and FPG were significantly lower in the group with more severe obesity compared to the group of obesity class I patients.

Hsu et al.[49] analysed patients with BMI < 35 kg/m<sup>2</sup> and T2DM that underwent bariatric surgery (RYGB and SG) and compared them to a group with matched characteristics that underwent medical treatment. Complete remission was defined as FPG < 110 mg/dL and HbA1C < 6.0% with no use of medication and partial remission was defined as FPG 110–126 mg/dL and HbA1C 6.0–6.5% without medication. HbA1C reduction after 5 years of follow-up was significantly higher in the surgical group, as well as partial and complete remission (28% vs. 1.6% and 36% vs. 1.2%, respectively).

Lee et al.[50] compared the outcomes of bariatric surgery in non-obese ( $\text{BMI} < 30 \text{ kg/m}^2$ ) Asian patients with T2DM and obese ( $\text{BMI} > 30 \text{ kg/m}^2$ ) Asian patients with T2DM and investigated the predictors of T2DM remission. The definition for total remission was  $\text{HbA1C} < 6.0\%$  with no use of medication and for partial remission was  $\text{HbA1C} < 6.5\%$  with no medication. 1 year after surgery non-obese patients had total remission rates of 25% and partial remission rates of nearly 50%. Compared to obese subjects the total remission rates were lower. The ABCD Score was used, and proved to predict T2DM remission in non-obese patients.

Dixon et al.[4] analysed the outcomes of a new GB system, “LAP BAND”, in patients with BMI between 30-40. Only 5 patients with T2DM were included and 4 were using medication at baseline. After 5 years of follow-up all were off medication and significant decreases in both HbA1C and FPG were reported for all patients.

Bariatric surgery has also been suggested for adolescents[51-53], particularly if comorbidities are present – for instance, T2DM with onset during adolescence is more aggressive than if it has onset during adulthood[52] and disease control is harder to achieve.[52] It seems to have greater potential to induce weight loss and revert the obesity related comorbidities in this age group than in adults, mainly in the short to medium term.[51-53] However, there are still not many studies of long term outcomes in this age group.[51-53] The most used bariatric procedures used in adolescents are, similarly to adults, RYGB and SG[51, 53] – RYGB has some advantage compared to SG because of its reversibility.[53]

Inge et al.[51] studied adolescents ( $\text{age} \leq 19$  years) with  $\text{BMI} > 30 \text{ kg/m}^2$  that underwent bariatric surgery (RYGB and SG). A significant weight loss was obtained for both procedures. Among adolescents with T2DM, the remission rates reached 95% at 3 years of follow-up and prediabetes had remission rates of over 75%.

Vilallonga et al.[53] studied the outcomes of RYGB in obese ( $\text{BMI} > 40 \text{ kg/m}^2$  or  $\text{BMI} > 35 \text{ kg/m}^2$  with an associated comorbidity) adolescents ( $\text{age} < 18$  years). 19 adolescents were paired with a matched control group of adults, with a mean follow-up  $> 7$  years in both groups. All patients with T2DM in both groups achieved remission.

Aminian et al.[22] analysed the metabolic outcomes in patients with failed bariatric surgery (patients that didn't achieve %EWL of at least 25% after a follow-up of 5 years or more) and they concluded that although bariatric surgery was not successful in achieving a significant and sustained weight loss in some patients, it kept its advantages regarding not only T2DM – with a remission rate of 23% and a clinical improvement in 42% of patients – but also in HBP and DLP (discussed ahead).



In studies with longer follow-up periods, a relapse of T2DM in patients that achieved remission was described[19] – with a 5 year relapse rate of up to one third of the patients that achieved remission after bariatric surgery[54], which can reach half of the patients with longer follow-up.[12, 29] This relapse is dependent of the age of the patients – higher relapse in older patients[54] – and also of the disease severity before surgical treatment – higher relapse rates among patients who had more advanced disease[25] (longer duration of disease[3, 11, 54], insulin use previously to surgery[54] and poorer preoperative glycemic control[54]). Other factors that influence this relapse have been detected in some studies, and include lower %EWL[3, 11] and weight regain (BMI increase  $\geq 5$  kg/m<sup>2</sup> compared to maximum weight loss achieved).[3, 11] This long term phenomenon highlights the importance of long term monitoring of diabetic patients that underwent a bariatric procedure in order to prevent relapse.[7, 14, 25, 29, 30] Some authors go further in these prevention measures and propose the use of metformin after bariatric procedures (because it has no risk of hypoglycaemia or weight gain).[25] However, even in patients with T2DM relapse after bariatric surgery, glycaemic control is easier to achieve[14], which translates in lower use of medication[11, 12, 14], and there are other metabolic improvements in both HBP and DLP[11] (revealed below).

Regarding health care costs, there aren't many studies that analysed this aspect of bariatric surgery because it requires studies with long term follow-up of diabetic patients that underwent bariatric surgery, which are still scarce.[14] According to Keating et al.[55] – who assessed the costs of bariatric surgery compared to medical treatment over a follow-up period of 15 years, based on the SOS study data –, it seems there is no significant difference between surgical and medical treatment in patients with T2DM.[14, 55] In patients with euglycaemia or prediabetes, the total health care costs are significantly higher for the surgical treatment.[14, 55] However, further investigations are needed to be able to accurately define which strategy is economically most advantageous.[14, 55]

Tang et al.[56] analysed the cost-effectiveness of bariatric surgery for T2DM compared to medical treatment. The bariatric procedures studied were RYGB and SG. This study concluded both procedures are cost-effective compared to medical treatment, with a slight advantage for SG. However, this study only considered a period of 2 years, so further studies regarding the long term costs of bariatric surgery are needed.

Some studies have suggested that bariatric surgery may have a protective effect on obese patients with impaired FPG, reducing the risk of developing T2DM.[10]

## HBP

Bariatric surgery achieved clinical improvements in HBP[3, 6, 18, 22, 28, 54], and has potential to revert this disease[28, 54] – defined as normal BP (sBP < 140 mmHg and dBP < 90 mmHg) without the use of antihypertensive medication. Remission rates 1 year after surgery are significant, with remission in around two thirds of patients [54] and only a minority of patients without improvement in BP levels at this point (around 10%)[54].

Pedersen et al.[6] analysed early BP changes following RYGB. They performed 24h ambulatory BP measurements in obese patients (BMI 35-50 kg/m<sup>2</sup>) preoperatively, 1 and 10 days after RYGB. 20 patients were studied, with a preoperative rate of HBP of 50%. Antihypertensive medication was maintained after surgery in patients with HBP. Baseline characteristics of both groups were similar. 1 day after surgery no difference was reported in dBP, sBP or MAP in both groups. 10 days after surgery there was a significant reduction in sBP for both groups, and dBP also decreased significantly in the preoperative HBP group, although there was a slight decrease in the normotensive group as well (p=0.058). MAP was also significantly lower in both study groups. No statistically significant differences were identified between the 2 groups in all the BP measurements made in the 3 moments evaluated. No relationship between weight change and 24h MAP change was found in any of the groups neither for the total population of the study.

Mingrone et al.[30], reported reductions in both dBP and sBP in all 3 groups studied (BPD, RYGB and medical treatment), but without statistical significance. The only significant difference was found in the medical group, which had a higher need for medication use than the 2 surgical groups at 5 years of follow-up. Yska et al.[27] also found a significant reduction in antihypertensive medication use following RYGB after 5 years of follow-up.

Schauer et al.[23] reported 3-year outcomes in 150 obese patients with poorly controlled T2DM randomized for RYGB, SG or medical therapy. No significant differences in BP levels were found among the 3 groups studied. Similarly to other studies, both surgical groups had a lower need for antihypertensive medication than the medical group. Schauer et al.[31] described the 5-year outcomes for this population and the same findings for HBP were found.

Yan et al.[7] reported, regarding BP, a significant reduction in sBP in the RYGB group, compared to the medical group, as well as a reduction in antihypertensive medication use. No significant difference in dBP was found in both groups.

Article	Type of study	Number of patients	Surgical procedures studied	Follow-up period	Significant changes found
Pedersen et al.[6]	Prospective	22	RYGB	1 day	No changes
		20		10 days	Decrease in sBP and MAP; Decrease in dBP in patients with preoperative HBP
Mingrone et al.[30]	RCT	60	BPD, RYGB	5 years	Lower need for antihypertensive medication following surgery
Yska et al.[27]	Retrospective	569	RYGB, SG, GB	1 year	Significant reductions in BP levels following RYGB
				5 years	Lower need for antihypertensive medication following RYGB
Schauer et al.[23]	RCT	137	RYGB, SG	3 years	Lower need for antihypertensive medication following surgery
Schauer et al.[31]	RCT	134	RYGB, SG	5 years	Lower need for antihypertensive medication following surgery
Yan et al.[7]	Meta-analysis	410	RYGB	1 – 5 years	Significant reductions in sBP and medication use following RYGB
Shoar et al.[32]	Meta-analysis	552	RYGB, SG	> 3 years	HBP remission in $\approx$ 62% following RYGB and $\approx$ 57% following SG
Li et al.[8]	Meta-analysis	1 552	RYGB, SG	1.5 – 60 months	HBP remission in 60% following RYGB and $\approx$ 51% following SG
Liu et al.[35]	Prospective	140	SG	5 years	Clinical improvement of HBP in $\approx$ 50% of patients
Celik et al.[37]	Retrospective	121	DSIT	18 months <sup>a</sup>	HBP remission $\approx$ 95% in patients with BMI > 35 kg/m <sup>2</sup> , T2DM and HBP

Table IV – Overview of HBP changes reported in the articles analysed

a – Only mean follow-up was reported.

Shoar et al.[32] compared mid and long-term outcomes for RYGB and SG, has shown no significant differences in HBP remission between RYGB and SG in both periods.

On the contrary, Li et al. [8] analysed 21 studies that mentioned HBP remission, and found significantly higher remission rates for RYGB compared to SG.

Liu et al.[35] reported clinical improvements after SG in around 50% of the patients with HBP.

Courcoulas et al.[36] reported better results for RYGB than GB in HBP remission.

The study by Celik et al.[37] analysing metabolic outcomes following DSIT, detected a remission rate of around 95% in patients with BMI > 35 kg/m<sup>2</sup>, T2DM and HBP.

Table IV presents a summary of the articles studied and the main information reported regarding HBP outcomes.

Similarly to T2DM, some studies have analysed the outcomes of bariatric surgery on mildly obese patients.

The RCT by Cummings et al.[45] has also shown significant decrease in sBP after RYGB compared to ILMI, but it reported no significant change in dBP in both groups.

Courcoulas et al.[46] published a RCT that has shown improvements in both sBP and dBP. Decrease in sBP was more significant for RYGB compared to GB and LWLI 3 years after treatment and decrease in dBP was more significant for RYGB compared to GB 3 years after surgery.

Another RCT by Ikramuddin et al.[47] has shown that RYGB led to a lower need of antihypertensive medication and a significant reduction in dBP compared to medical treatment at 1 year of follow-up. The paper by Ikramuddin et al.[48] reported lower mean BP in the RYGB group and although the proportion of patients that achieved sBP < 130 mmHg was not significantly different in both groups, there was a significant higher number of patients that achieved this BP goal in the RYGB group with no use of medication.

The article by Dixon et al.[4] has reported a sustained decrease in sBP from 1 to 5 years of follow-up after GB in patients with BMI 30-40 kg/m<sup>2</sup> and a reduction in antihypertensive medication use at 5 years of follow-up.

The factors that have been described to predict this remission are related to the severity of the disease: lower number of antihypertensive medications used prior to surgery and shorter duration of disease are associated with higher remission rates.[54] Younger age has also been described as a predictor of remission but that finding is not consensual among studies.[54] The surgical procedure doesn't seem to affect these outcomes (RYGB vs. SG vs. GB).[54]

Even if remission is not obtained, there is a significant improvement in both dBP and sBP after bariatric surgery.[11]

As described for T2DM, bariatric surgery seems to have great potential in reverting obesity related comorbidities in adolescents.[51-53]

Inge et al.[51] has reported a remission rate for HBP of nearly 75% in obese adolescents 3 years after either RYGB or SG.

Similarly, Vilallonga et al.[53] studied the outcomes of RYGB in obese adolescents paired with a matched control group of adults. All patients with HBP in both groups achieved remission 7 years after surgery.

In the context of failed bariatric surgery ( $\%EWL < 25\%$  after a follow-up  $\geq 5$  years), these beneficial effects are still present, as reported by Aminian et al.[22] where there was a significant reduction in sBP after failed bariatric surgery, with 58% of patients achieving the treatment goals defined by the ADA –  $sBP < 130$  mmHg and  $dBP < 80$  mmHg.

A relapse of HBP in patients that achieved remission after surgery has been described[54], with relapse rates of around 20% after 3 years of follow-up.[54] This relapse is associated with a higher number of antihypertensive medications used prior to surgery[54], lower  $\%EWL$  in the 1<sup>st</sup> year after bariatric surgery[54] and weight regain.[3]

Additionally, bariatric surgery seems to have a protective effect on obese patients without HBP prior to surgery.[54]

## **DLP**

Bariatric surgery has been shown to induce clinical improvements in patients with DLP[3, 5, 18, 22, 28], sometimes achieving reversion of this disease – normal plasma lipids profile without the use of medication.[9, 28, 37]

Some studies have shown significant reduction in TG and LDL levels, as well as a significant increase of HDL levels.[3, 11]

Carswell et al.[9] studied the effect of RYGB on plasma lipid levels and reported significant decreases in total cholesterol levels (from the 1<sup>st</sup> month after surgery up to 2 years of follow-up), LDL cholesterol levels (from the 1<sup>st</sup> month after surgery up to 2 years of follow-up) and TG levels (from the 3<sup>rd</sup> month after surgery up to 2 years of follow-up) and significant increases in HDL cholesterol levels (from 12 months after surgery up to 2 years of follow-up) and NEFA (from the 1<sup>st</sup> month after surgery until the 3<sup>rd</sup> month of follow-up, with no further changes compared to preoperative levels). This paper compared the effects of statins and RYGB and concluded that the surgical procedure had more favourable effects than the pharmacological therapy – statins can lower total cholesterol, LDL and TG levels up to 20%, 28% and 13%, respectively, and increase HDL up to 5% vs. a reduction of total cholesterol, LDL and TG of 16%, 21% and 36%, respectively, and 11% increase in HDL following RYGB.

Mingrone et al.[30] compared BPD, RYGB and medical treatment and found significant differences for the surgical groups in reducing total cholesterol, LDL and TG levels comparably to the medical group, particularly after BPD. Increase in HDL levels was reported in all 3 groups, with a more pronounced effect after RYGB.

Yska et al.[27] found significant reductions in TG levels 1 year after RYGB compared to medical treatment. After 5 years of follow-up there was a significant reduction in lipid-lowering medication following RYGB.

Yan et al.[7] detected reductions in TG and LDL and increase in HDL following RYGB, compared to the medical group, as well as lower lipid-lowering medication use.

Nosso et al.[33] compared RYGB and SG and only found significant decreases in total cholesterol and LDL following RYGB.

Article	Type of study	Number of patients	Surgical procedures studied	Follow-up period	Significant changes found
Carswell et al.[9]	Meta-analysis	7 815	RYGB	1 – 48 months	Sustained decreases in total cholesterol, LDL and TG; Sustained increase in HDL and temporary increase in NEFA
Mingrone et al.[30]	RCT	60	BPD, RYGB	5 years	Reduction of total cholesterol, LDL and TG and increase of HDL
Yska et al.[27]	Retrospective	569	RYGB, SG, GB	1 year	Decrease in TG levels
				5 years	Lower need for lipid-lowering medication following surgery
Yan et al.[7]	Meta-analysis	410	RYGB	1 – 5 years	Significant reductions in TG and LDL, increase of HDL and lower lipid-lowering medication use following RYGB
Nosso et al.[33]	Meta-analysis	552	RYGB, SG	> 3 years	Decreases in total cholesterol and LDL following RYGB
Li et al.[8]	Meta-analysis	1 269	RYGB, SG	1.5 – 60 months	DLP remission in $\approx$ 71% following RYGB and $\approx$ 50% following SG
Schauer et al.[23]	RCT	137	RYGB, SG	3 years	Significant reductions in TG and increase of HDL and lower lipid-lowering medication use following surgery
Schauer et al.[31]	RCT	134	RYGB, SG	5 years	
Shoar et al.[32]	Meta-analysis	798	RYGB, SG	> 3 years	DLP remission in $\approx$ 55% following RYGB and $\approx$ 48% following SG and hyper-TG remission in $\approx$ 58% following RYGB and SG
Griffo et al.[34]	Prospective	25	RYGB, SG	2 weeks	Reductions in fasting total cholesterol, TG, LDL and HDL levels and in postprandial total cholesterol, TG and HDL levels
Liu et al.[35]	Prospective	140	SG	5 years	Clinical improvement of DLP in > 45% of patients
Courcoulas et al.[36]	Prospective	2 348	RYGB, GB	3 years	DLP remission in $\approx$ 62% following RYGB and $\approx$ 27% following GB, Low HDL remission in $\approx$ 86% following RYGB and $\approx$ 68% following GB and hyper-TG remission in $\approx$ 86% following RYGB and $\approx$ 62% following GB
Celik et al.[37]	Retrospective	144	DSIT	1 year	Decreases in TG, LDL and VLDL; DLP remission > 90% in patients with BMI > 35 kg/m <sup>2</sup> , T2DM and DLP

Table V – Summary of DLP changes reported in the articles studied

Li et al.[8] compared DLP remission following RYGB and SG, and found superiority for RYGB in inducing DLP remission.

Schauer et al.[23] reported 3-year outcomes in 150 obese patients with poorly controlled T2DM randomized for RYGB, SG or intensive medical therapy. Significant reduction in TG and increase in HDL in both surgical groups compared to the medical group was found, as well as a lower need for lipid-lowering medication in both surgical groups. The complementary publication[31] reporting the 5-year outcomes for this population showed no differences between the 2 periods.

Shoar et al.[32] compared mid and long-term outcomes for RYGB and SG and found no significant differences in DLP remission between RYGB and SG in both periods. Additionally, there were some studies that analysed the mid-term effects of these procedures in TG levels, and no difference was found between RYGB and SG for mid-term reduction of TG.

Griffo et al.[34] described reductions in fasting total cholesterol, TG, LDL and HDL and in postprandial total cholesterol, TG and HDL levels 2 weeks after surgery, with no difference between RYGB and SG. The authors reported that the short term decrease in HDL was later compensated, with an overall increase in HDL 1 year after surgery.

Liu et al.[35] found clinical improvements in plasma lipid levels in over 45% of patients with DLP following SG.

Courcoulas et al.[36] detected better results following RYGB than the ones obtained after GB in DLP reversion, with significant decrease in TG and increase in HDL for both procedures.

Celik et al.[37] analysed metabolic outcomes following DSIT and found significant decreases in LDL, VLDL and TG after 1 year of follow-up and a remission rate of DLP over 90% for patients that underwent DSIT who had preoperative BMI > 35kg/m<sup>2</sup>, T2DM and DLP.

Table V presents a summary of the articles analysed and the main information obtained regarding DLP outcomes.

No predictors for DLP remission were described in any of the papers analysed.

Like in T2DM and HBP, some studies analysed DLP outcomes after bariatric surgery in mildly obese patients (BMI < 35 kg/m<sup>2</sup>).



The RCT by Cummings et al.[45] reported reductions of TG in both RYGB and ILMI groups with no significant differences, as well as an increase of HDL in both groups, with a borderline non-significant difference between RYGB and ILMI ( $p=0.08$ ). Total cholesterol and LDL were not altered in both groups.

Courcoulas et al.[46] issued a RCT that also detected a more significant reduction of TG and increase of HDL in RYGB compared to LWLI, with no significant differences for any other plasma lipid levels between the 3 treatments studied (RYGB, GB and LWLI).

Ikramuddin et al.[47] published another RCT that reported lower need of lipid-lowering medication in the RYGB compared to the medical treatment group, as well as a reduction of TG and increase of HDL after 1 year of follow-up. The paper with the 2 year outcomes by Ikramuddin et al.[48] only reported no difference in LDL levels between the 2 groups, but with a higher number of patients in the RYGB group achieving  $LDL < 100$  mg/dL with no use of medication.

Dixon et al.[4] reported a higher prevalence of normal plasma levels for TG and HDL and a reduction in the use of lipid-lowering medications 5 years after GB.

Comparably to what is described for both T2DM and HBP, bariatric surgery in adolescents has very good outcomes on DLP.[51-53]

Inge et al.[51] has reported a remission rate of DLP among adolescent patients that underwent either RYGB or SG superior to 65% after 3 years of follow-up, with a substantial improvement in all patients with baseline DLP in the same period.

Likewise, Vilallonga et al.[53] studied the outcomes of RYGB in obese adolescents paired with a matched control group of adults and found that all patients with DLP in both groups achieved remission 7 years after surgery.

This disease, as both the other diseases approached in the present paper, shows improvements after failed bariatric surgery ( $\%EWL < 25\%$  after a follow-up  $\geq 5$  years), with Aminian et al.[22] reporting a significant reduction of TG after failed bariatric surgery and 68% of patients achieving the ADA goals for cholesterol – LDL levels  $< 100$  mg/dL.

## DISCUSSION

Bariatric surgery has proven to be superior to optimal medical treatment for T2DM, HBP and DLP treatment in obese patients, from mild obesity to morbid obesity.

Among the comorbidities studied, T2DM outcomes after bariatric surgery are the best studied and that justifies already including bariatric surgery as a therapeutic option for severely obese patients with T2DM in most recommendations for T2DM treatment. Regarding this obesity related comorbidity, most predictors have been established and there are even validated predictive scores for remission. The most consensual predictors of remission include disease severity criteria, like duration of disease and preoperative C-peptide levels, HbA1C levels and insulin use, and the surgical procedure used, with controversy for the 2 most used bariatric surgery procedures, RYGB and SG. Some studies show superiority of RYGB but others show no significant difference, although RYGB presents with higher remission rates. BMI is used as both a criteria of eligibility for bariatric surgery and a predictor of T2DM remission but remission seems to be only higher for very high BMI values, whereas abdominal circumference may have a better association with remission. However, further studies are needed before abdominal circumference can be considered a suitable replacement for BMI.

The next step may be expanding the recommendations of bariatric surgery as a treatment for T2DM to mildly obese patients (BMI 30–35 kg/m<sup>2</sup>) since superiority of bariatric surgery to medical treatment has been shown in this population group, although some more information on long term outcomes is still needed.

Besides only finding 1 study in non-obese patients for the present paper, that study used the BMI threshold for obesity of 30 kg/m<sup>2</sup> when analysing an Asian population, which may in fact correspond to an obese population, so this is a group of patients in which there's almost no information to even think about suggesting bariatric surgery as a T2DM treatment.

In terms of health costs, there's little information and only for T2DM. Bariatric surgery's superiority to medical treatment is not established, so further studies are needed. When comparing surgical procedures, the only study analysed found a slight advantage for SG.

HBP and DLP outcomes after bariatric surgery have been less studied than T2DM outcomes, but there's substantial evidence that bariatric surgery is a treatment option for these comorbidities with great results. Effect on HBP is more pronounced for sBP and improvements in BP levels are well described. As for DLP, the main effects of bariatric surgery seem to be the reduction in TG, total cholesterol and LDL cholesterol levels and an increase in HDL cholesterol levels, although the evidence is better for TG and HDL changes than for the rest of the lipid profile values.

Bariatric surgery has also shown to decrease the need for medication in all of these 3 comorbidities.

Another important aspect of bariatric surgery is that it has shown to prevent HBP in normotensive patients.

In HBP and DLP, similarly to T2DM, bariatric surgery has shown to be more effective than medical treatment in mildly obese patients, with outcomes comparable to the ones in more severely obese patients.

Regarding predictors for remission of these 2 comorbidities information is very little to none. Further studies are needed to establish those predictors like it was done for T2DM.

Health care costs of bariatric surgery as a treatment for these comorbidities is also unknown presently and this will be an important aspect that will have to be studied if bariatric surgery is to be considered a therapeutic option in the future.

As a therapeutic option for adolescents, bariatric surgery seems to have great results as a treatment for T2DM, HBP and DLP but there's still very little information and further studies on the outcomes of bariatric surgery in this population are needed. RYGB may be more advantageous in this age group compared to SG for being a potentially reversible procedure, especially until the long term effects of these surgeries are disclosed.

The 2 most used procedures, RYGB and SG, have very good results as a treatment for obesity and related comorbidities. There's still some controversy regarding whether RYGB is superior to SG, with different findings for different studies. It seems that, if different, they are not very different. Although RYGB presents higher remission rates than SG, in many cases the difference is not statistically significant. Therefore, the choice between these two procedures may be less dependent of the outcomes wanted and instead be motivated by other factors.

Other procedures are less used because they have a risk-benefit ratio that is not as advantageous as it is for RYGB and SG. For instance, BPD seems to have better results than RYGB and SG but is also associated with more complications and GB has worse results reported than RYGB and SG and, although less invasive, has a high need of reoperation and removal.

Some less used procedures and some newly proposed procedures – DSIT, SIPS surgery or endoscopic procedures – have shown promising results but further investigation is needed to establish their role in treatment algorithms for obesity and related comorbidities.

## CONCLUSION

Apart from all the advantages in managing obesity, bariatric surgery is an effective treatment for obesity related comorbidities.

Evidence of these benefits for T2DM has allowed bariatric surgery to be included in the treatment algorithms for this disease. With the evidence available currently, it's even possible to predict with considerable accuracy which patients will best respond to this therapeutic approach.

For HBP and DLP promising results are also described and in the future this therapeutic approach can be included in the treatment strategies for those diseases, as has happened for T2DM.

By reducing the need for medication for all these comorbidities, bariatric surgery shows to have great potential in achieving better control of these diseases than the one we achieve currently.

The protective effect for HBP described after bariatric surgery may even allow us to use it as a prophylactic measure in patients with other indications for these surgical procedures.

All these findings support the claim that bariatric surgery has a significant impact in cardiovascular risk factors, with a great potential to minimize some of the greatest health problems presently.

Bariatric surgery's superiority to the best alternative treatment available has been well established and so it's important to continue researching this field in order to better establish the benefits of this therapeutic approach and also to determine who are the ones who can benefit the most from it.

## REFERENCES

1. Organization, W.H., *Global report on diabetes*. 2016: World Health Organization.
2. Organization, W.H., *A global brief on hypertension: silent killer, global public health crisis: World Health Day 2013*. 2013.
3. Corcelles, R., C.R. Daigle, and P.R. Schauer, *MANAGEMENT OF ENDOCRINE DISEASE: Metabolic effects of bariatric surgery*. Eur J Endocrinol, 2016. **174**(1): p. R19-28.
4. Dixon, J.B., et al., *LAP-BAND for BMI 30-40: 5-year health outcomes from the multicenter pivotal study*. Int J Obes (Lond), 2016. **40**(2): p. 291-8.
5. Eligar, V.S. and A.K. Narayanaswamy, *Bariatric surgery and remission of type 2 diabetes mellitus*. Curr Opin Lipidol, 2016. **27**(1): p. 97-8.
6. Pedersen, J.S., et al., *Early 24-hour blood pressure response to Roux-en-Y gastric bypass in obese patients*. Scand J Clin Lab Invest, 2016. **77**(1): p. 53-59.
7. Yan, Y., et al., *Roux-en-Y Gastric Bypass Versus Medical Treatment for Type 2 Diabetes Mellitus in Obese Patients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials*. Medicine (Baltimore), 2016. **95**(17): p. e3462.
8. Li, J., D. Lai, and D. Wu, *Laparoscopic Roux-en-Y Gastric Bypass Versus Laparoscopic Sleeve Gastrectomy to Treat Morbid Obesity-Related Comorbidities: a Systematic Review and Meta-analysis*. Obes Surg, 2016. **26**(2): p. 429-42.
9. Carswell, K.A., et al., *A Systematic Review and Meta-analysis of the Effect of Gastric Bypass Surgery on Plasma Lipid Levels*. Obes Surg, 2016. **26**(4): p. 843-55.
10. Campos, J., et al., *THE ROLE OF METABOLIC SURGERY FOR PATIENTS WITH OBESITY GRADE I AND CLINICALLY UNCONTROLLED TYPE 2 DIABETES*. Arq Bras Cir Dig, 2016. **0**: p. 0.
11. Brethauer, S.A., et al., *Can diabetes be surgically cured? Long-term metabolic effects of bariatric surgery in obese patients with type 2 diabetes mellitus*. Ann Surg, 2013. **258**(4): p. 628-36; discussion 636-7.
12. Brito, J.P., V.M. Montori, and A.M. Davis, *Metabolic Surgery in the Treatment Algorithm for Type 2 Diabetes: A Joint Statement by International Diabetes Organizations*. Jama, 2017. **317**(6): p. 635-636.

13. Celio, A.C. and W.J. Pories, *A History of Bariatric Surgery: The Maturation of a Medical Discipline*. Surg Clin North Am, 2016. **96**(4): p. 655-67.
14. Amouyal, C. and F. Andreelli, *What is the evidence for metabolic surgery for type 2 diabetes? A critical perspective*. Diabetes Metab, 2017. **43**(1): p. 9-17.
15. Roslin, M.S., C. Cripps, and A. Peristeri, *Bariatric and metabolic surgery: current trends and what's to follow*. Curr Opin Gastroenterol, 2015. **31**(6): p. 513-8.
16. Cho, J.M., et al., *Effect of sleeve gastrectomy on type 2 diabetes as an alternative treatment modality to Roux-en-Y gastric bypass: systemic review and meta-analysis*. Surg Obes Relat Dis, 2015. **11**(6): p. 1273-80.
17. Vidal, J., et al., *Metabolic Surgery in Type 2 Diabetes: Roux-en-Y Gastric Bypass or Sleeve Gastrectomy as Procedure of Choice?* Curr Atheroscler Rep, 2015. **17**(10): p. 58.
18. Chen, Y., et al., *Impact of roux-en Y gastric bypass surgery on prognostic factors of type 2 diabetes mellitus: meta-analysis and systematic review*. Diabetes Metab Res Rev, 2014. **31**(7): p. 653-62.
19. Abbasi, J., *Unveiling the "Magic" of Diabetes Remission After Weight-Loss Surgery*. Jama, 2017. **317**(6): p. 571-574.
20. Genser, L., et al., *Obesity, Type 2 Diabetes, and the Metabolic Syndrome: Pathophysiologic Relationships and Guidelines for Surgical Intervention*. Surg Clin North Am, 2016. **96**(4): p. 681-701.
21. Mayor, S., *Bariatric surgery should be an option for treating type 2 diabetes, societies say*. Bmj, 2016. **353**: p. i2955.
22. Aminian, A., et al., *Failed Surgical Weight Loss Does Not Necessarily Mean Failed Metabolic Effects*. Diabetes Technol Ther, 2015. **17**(10): p. 682-4.
23. Schauer, P.R., et al., *Bariatric surgery versus intensive medical therapy for diabetes--3-year outcomes*. N Engl J Med, 2014. **370**(21): p. 2002-13.
24. Smeu, B., et al., *Early Improvement in Glycemic Metabolism after Laparoscopic Sleeve Gastrectomy in Obese Patients - A Prospective Study*. Chirurgia (Bucur), 2015. **110**(5): p. 430-9.
25. Arterburn, D. and D. McCulloch, *Bariatric Surgery for Type 2 Diabetes: Getting Closer to the Long-term Goal*. Jama, 2016. **315**(12): p. 1276-7.

26. Panunzi, S., et al., *Determinants of Diabetes Remission and Glycemic Control After Bariatric Surgery*. Diabetes Care, 2015. **39**(1): p. 166-74.
27. Yska, J.P., et al., *Remission of Type 2 Diabetes Mellitus in Patients After Different Types of Bariatric Surgery: A Population-Based Cohort Study in the United Kingdom*. JAMA Surg, 2015. **150**(12): p. 1126-33.
28. Fouse, T. and S. Brethauer, *Resolution of Comorbidities and Impact on Longevity Following Bariatric and Metabolic Surgery*. Surg Clin North Am, 2016. **96**(4): p. 717-32.
29. Dixon, J.B., *Obesity in 2015: Advances in managing obesity*. Nat Rev Endocrinol, 2016. **12**(2): p. 65-6.
30. Mingrone, G., et al., *Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial*. Lancet, 2015. **386**(9997): p. 964-73.
31. Schauer, P.R., et al., *Bariatric Surgery versus Intensive Medical Therapy for Diabetes - 5-Year Outcomes*. N Engl J Med, 2017. **376**(7): p. 641-651.
32. Shoar, S. and A.A. Saber, *Long-term and midterm outcomes of laparoscopic sleeve gastrectomy versus Roux-en-Y gastric bypass: a systematic review and meta-analysis of comparative studies*. Surg Obes Relat Dis, 2016. **13**(2): p. 170-180.
33. Nosso, G., et al., *Comparative Effects of Roux-en-Y Gastric Bypass and Sleeve Gastrectomy on Glucose Homeostasis and Incretin Hormones in Obese Type 2 Diabetic Patients: A One-Year Prospective Study*. Horm Metab Res, 2016. **48**(5): p. 312-7.
34. Griffo, E., et al., *Early improvement of postprandial lipemia after bariatric surgery in obese type 2 diabetic patients*. Obes Surg, 2014. **24**(5): p. 765-70.
35. Liu, S.Y., et al., *Long-term Results on Weight Loss and Diabetes Remission after Laparoscopic Sleeve Gastrectomy for A Morbidly Obese Chinese Population*. Obes Surg, 2015. **25**(10): p. 1901-8.
36. Courcoulas, A.P., et al., *Weight change and health outcomes at 3 years after bariatric surgery among individuals with severe obesity*. Jama, 2013. **310**(22): p. 2416-25.
37. Celik, A., et al., *Metabolic Outcomes of Laparoscopic Diverted Sleeve Gastrectomy with Ileal Transposition (DSIT) in Obese Type 2 Diabetic Patients*. Obes Surg, 2015. **25**(11): p. 2018-22.

38. Panunzi, S., et al., *Predictors of remission of diabetes mellitus in severely obese individuals undergoing bariatric surgery: do BMI or procedure choice matter? A meta-analysis*. Ann Surg, 2015. **261**(3): p. 459-67.
39. Palmisano, S., et al., *Preoperative Predictive Factors of Successful Weight Loss and Glycaemic Control 1 Year After Gastric Bypass for Morbid Obesity*. Obes Surg, 2015. **25**(11): p. 2040-6.
40. Park, J.Y. and Y.J. Kim, *Prediction of Diabetes Remission in Morbidly Obese Patients After Roux-en-Y Gastric Bypass*. Obes Surg, 2015. **26**(4): p. 749-56.
41. Zenti, M.G., et al., *Clinical factors that predict remission of diabetes after different bariatric surgical procedures: interdisciplinary group of bariatric surgery of Verona (G.I.C.O.V.)*. Acta Diabetol, 2015. **52**(5): p. 937-42.
42. Lee, W.J., et al., *Predicting success of metabolic surgery: age, body mass index, C-peptide, and duration score*. Surg Obes Relat Dis, 2013. **9**(3): p. 379-84.
43. Still, C.D., et al., *Preoperative prediction of type 2 diabetes remission after Roux-en-Y gastric bypass surgery: a retrospective cohort study*. Lancet Diabetes Endocrinol, 2014. **2**(1): p. 38-45.
44. Xu, L., et al., *Effectiveness of laparoscopic Roux-en-Y gastric bypass on obese class I type 2 diabetes mellitus patients*. Surg Obes Relat Dis, 2015. **11**(6): p. 1220-6.
45. Cummings, D.E., et al., *Gastric bypass surgery vs intensive lifestyle and medical intervention for type 2 diabetes: the CROSSROADS randomised controlled trial*. Diabetologia, 2016. **59**(5): p. 945-53.
46. Courcoulas, A.P., et al., *Three-Year Outcomes of Bariatric Surgery vs Lifestyle Intervention for Type 2 Diabetes Mellitus Treatment: A Randomized Clinical Trial*. JAMA Surg, 2015. **150**(10): p. 931-40.
47. Ikramuddin, S., et al., *Roux-en-Y gastric bypass vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia: the Diabetes Surgery Study randomized clinical trial*. Jama, 2013. **309**(21): p. 2240-9.
48. Ikramuddin, S., et al., *Roux-en-Y gastric bypass for diabetes (the Diabetes Surgery Study): 2-year outcomes of a 5-year, randomised, controlled trial*. Lancet Diabetes Endocrinol, 2015. **3**(6): p. 413-22.
49. Hsu, C.C., et al., *Effect of Bariatric Surgery vs Medical Treatment on Type 2 Diabetes in Patients With Body Mass Index Lower Than 35: Five-Year Outcomes*. JAMA Surg, 2015. **150**(12): p. 1117-24.



50. Lee, W.J., et al., *The Effect and Predictive Score of Gastric Bypass and Sleeve Gastrectomy on Type 2 Diabetes Mellitus Patients with BMI < 30 kg/m(2)*. *Obes Surg*, 2015. **25**(10): p. 1772-8.
51. Inge, T.H., et al., *Weight Loss and Health Status 3 Years after Bariatric Surgery in Adolescents*. *N Engl J Med*, 2016. **374**(2): p. 113-23.
52. Beamish, A.J., *Bariatric surgery for obese adolescents to prevent type 2 diabetes*. *Bmj*, 2016. **353**: p. i2977.
53. Vilallonga, R., J. Himpens, and S. van de Vrande, *Long-Term (7 Years) Follow-Up of Roux-en-Y Gastric Bypass on Obese Adolescent Patients (<18 Years)*. *Obes Facts*, 2016. **9**(2): p. 91-100.
54. Benaiges, D., et al., *Predictors of Hypertension Remission and Recurrence After Bariatric Surgery*. *Am J Hypertens*, 2016. **29**(5): p. 653-9.
55. Keating, C., et al., *Health-care costs over 15 years after bariatric surgery for patients with different baseline glucose status: results from the Swedish Obese Subjects study*. *Lancet Diabetes Endocrinol*, 2015. **3**(11): p. 855-65.
56. Tang, Q., et al., *Cost-Effectiveness of Bariatric Surgery for Type 2 Diabetes Mellitus: A Randomized Controlled Trial in China*. *Medicine (Baltimore)*, 2016. **95**(20): p. e3522.